Attorney's Docket No. CV0244

CHAPTER II

TRANSMITTAL LETTER TO THE UNITED STATES ELECTED OFFICE (EO/US)

(ENTRY INTO U.S. NATIONAL PHASE UNDER CHAPTER II)

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/EP98/00526	22/01/1998	25/01/1997

TITLE OF INVENTION

MULTI-DOSE WOUND GEL

APPLICANT(S)

Waring, Michael J.; Jacques, Elizabeth

Box PCT
Assistant Commissioner for Patents
Washington D.C. 20231

ATTENTION: EO/US

NOTE: The completion of those filing requirements that can be made at a time later than 30 months from the priority date results from the Commissioner exercising his judgment under the authority granted under 35 USC 371(d). The filing receipt will show the actual date of receipt of the last item completing the entry into the national phase. See 37 CFR 1.491 which states: "An international application enters the national state when the applicant has filed the documents and fees required by 35 USC 371(c) within the periods set forth in § 1.494 and § 1.495."

***WARNING:** Where the items are those which can be submitted to complete the entry of the international application into the national phase are subsequent to 30 months from the priority date the application is still considered to be in the international state and if mailing procedures are utilized to obtain a date the express mail procedure of 37 CFR 1.10 must be used (since international application papers are not covered by an ordinary certificate of mailing - 37 CFR 1.8 (2) (xi)).*

NOTE: Documents and fees must be clearly identified as a submission to enter the national state under 35 USC 371 otherwise the submission will be considered as being made under 35 USC 111. 37 CFR 1.494(f).

CERTIFICATION UNDER 37 CFR 1.10

I hereby certify that this Transmittal Letter and the papers indicated as being transmitted therewith is being deposited with the United States Postal Service on this date July 19, 1999, in an envelope as "Express Mail Post Office to Addressee" Mailing Label Number EM325661793US, addressed to the: Assistant Commissioner for Patents, Washington, D.C. 20231.

James Klein

(type or print name of person mailing paper)

Signature of person mailing paper

NOTE: Each paper or fee referred to as enclosed herein has the number of the "Express Mail" mailing label placed thereon prior to mailing. 37 CFR 1.16(b).

***WARNING:** Certificate of mailing (first class) or facsimile transmission procedures of 37 CFR 1.8 cannot be used to obtain a date of mailing or transmission for this correspondence.*

I. Applicant herewith submits to the United States Elected Office (EO/US) the following items under 35 U.S.C. 371:

a. ☒ This express request to immediately begin national examination procedures (35 U.S.C. 371(f)).

b. ☒ The U.S. National Fee (35 U.S.C. 371(c)(1)) and other fees (37 CFR 1.492) as indicated below:

2. Fees

CLAIMS FEE	(1) FOR	(2) NUMBER FILED	(3) NUMBER EXTRA	(4) RATE	(5) CALCULATIONS
☐*	TOTAL CLAIMS	12 -20=	- 0 -	x $18.00	$ - 0 -
	INDEPENDENT CLAIMS	6 -3=	3	x $78.00	234.00
	MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ $270.00	
BASIC FEE**	☐ U.S. PTO WAS INTERNATIONAL PRELIMINARY EXAMINATION AUTHORITY Where an international preliminary examination fee as set forth in § 1.482 has been paid on the international application to the U.S. PTO: ☐ and the international preliminary examination report states that the criteria of novelty, inventive step (non-obviousness) and industrial activity, as defined in PCT Article 33(1) to (4) have been satisfied for all the claims presented in the application entering the national stage (37 CFR 1.492(a)(4)) ..... $98.00 ☐ and the above requirements are not met (37 CFR 1.492(a)(1)) ..... $720.00 ☒ U.S. PTO WAS NOT INTERNATIONAL PRELIMINARY EXAMINATION AUTHORITY Where no international preliminary examination fee as set forth in § 1.482 has been paid to the U.S. PTO, and payment of an international search fee as set forth in § 1.445(a)(2) to the U.S. PTO: ☐ has been paid (37 CFR 1.492(a)(2)) .....$760. ☐ has not been paid (37 CFR 1.492(a)(3)) ..... $1,070.00 ☒ where a search report on the international application has been prepared by the European Patent Office or the Japanese Patent Office (37 CFR 1.492(a)(5)) .....$840.				840.00
	Total of above Calculations				= 1074.
SMALL ENTITY	Reduction by 1/2 for filing by small entity, if applicable. Affidavit must be filed also. (note 37 CFR 1.9, 1.27, 1.28)				-
	Subtotal				1074.
	Total National Fee				$ 1074.
	Fee for recording the enclosed assignment document $40.00 (37 CFR 1.21(h)). (See Item 13 below). See attached "ASSIGNMENT COVER SHEET".				
TOTAL	Total Fees enclosed				$ 1074.00

*See attached Preliminary Amendment Reducing the Number of Claims.

i. ☐ A check in the amount of _____ to cover the above fees is enclosed.

ii. ☒ Please charge Account No. 02-3869 in the amount of $ 1074.00. A duplicate copy of this sheet is enclosed.+

**WARNING:* *"To avoid abandonment of the application the applicant shall furnish to the United States Patent and Trademark Office not later than the expiration of 30 months from the priority date: * * * (2) the basic national fee (see § 1.492(a)). The 30-month time limit may not be extended." 37 CFR § 1.495(b).*

WARNING: *If the translation of the international application and/or the oath or declaration have not been submitted by the applicant within thirty (30) months from the priority date, such requirements may be met within a time period set by the Office. 37 CFR § 1.495(b)(2). The payment of the surcharge set forth in § 1.492(e) is required as a condition for accepting the oath or declaration later than thirty (30) months after the priority date. The payment of the processing fee set forth in § 1.492(f) is required for acceptance of an English translation later than thirty (30) months after the priority date. Failure to comply with these requirements will result in abandonment of the application. The provisions of § 1.136 apply to the period which is set. Notice of Jan. 3, 1993, 1147 O.G. 29 to 40.*

3. ☒ A copy of the International application as filed (35 U.S.C. 371(c)(2)):

NOTE: *Section 1.495 (b) was amended to require that the basic national fee and a copy of the international application must be filed with the Office by 30 months from the priority date to avoid abandonment. "The International Bureau normally provides the copy of the international application to the Office in accordance with PCT Article 20. At the same time, the International Bureau notifies applicant of the communication to the Office. In accordance with PCT Rule 47.1, that notice shall be accepted by all designated offices as conclusive evidence that the communication has duly taken place. Thus, if the applicant desires to enter the national stage, the applicant normally need only check to be sure the notice from the International Bureau has been received and then pay the basic national fee by 30 months from the priority date." Notice of Jan. 7, 1993, 1147 O.G. 29 to 40, at 35-36. See item 14c below.*

a. ☒ is transmitted herewith.

b. ☐ is not required, as the application was filed with the United States Receiving Office.

c. ☐ has been transmitted

i. ☐ by the International Bureau.
Date of mailing of the application (from form PCT/1B/308): _____.

ii. ☐ by applicant on _____.
Date

4. ☒ A translation of the International application into the English language (35 U.S.C. 371(c)(2)):

a. ☐ is transmitted herewith.

b. ☒ is not required as the application was filed in English.

c. ☐ was previously transmitted by applicant on _____
Date

d. ☐ will follow.

*See attached Preliminary Amendment Reducing the Number of Claims.

i. ☐ A check in the amount of _____ to cover the above fees is enclosed.

ii. ☒ Please charge Account No. 02-3869 in the amount of $ 1074.00. A duplicate copy of this sheet is enclosed.+

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WARNING: *If the translation of the international application and/or the oath or declaration have not been submitted by the applicant within thirty (30) months from the priority date, such requirements may be met within a time period set by the Office. 37 CFR § 1.495(b)(2). The payment of the surcharge set forth in § 1.492(e) is required as a condition for accepting the oath or declaration later than thirty (30) months after the priority date. The payment of the processing fee set forth in § 1.492(f) is required for acceptance of an English translation later than thirty (30) months after the priority date. Failure to comply with these requirements will result in abandonment of the application. The provisions of § 1.136 apply to the period which is set. Notice of Jan. 3, 1993, 1147 O.G. 29 to 40.*

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a. ☒ is transmitted herewith.

b. ☐ is not required, as the application was filed with the United States Receiving Office.

c. ☐ has been transmitted

i. ☐ by the International Bureau.
Date of mailing of the application (from form PCT/1B/308): _____.

ii. ☐ by applicant on _____.
Date

4. ☒ A translation of the International application into the English language (35 U.S.C. 371(c)(2)):

a. ☐ is transmitted herewith.

b. ☒ is not required as the application was filed in English.

c. ☐ was previously transmitted by applicant on _____.
Date

d. ☐ will follow.

5. ☒ Amendments to the claims of the International application under PCT Article 19 (35 U.S.C. 371(c)(3)):

NOTE: *The Notice of January 7, 1993 points out that 37 CFR § 1.495(a) was amended to clarify the existing and continuing practice that PCT Article 19 amendments must be submitted by 30 months from the priority date and this deadline may not be extended. The Notice further advises that: "The failure to do so will not result in loss of the subject matter of the PCT Article 19 amendments. Applicant may submit that subject matter in a preliminary amendment filed under section 1.121. In many cases, filing an amendment under section 1.121 is preferable since grammatical or idiomatic errors may be corrected." 1147 O.G. 29-40, at 36.*

a. ☐ are transmitted herewith.

b. ☐ have been transmitted

i. ☐ by the International Bureau.
Date of mailing of the amendment (from form PCT/1B/308): _____.

ii. ☐ by applicant on (date) _____.
Date

c. ☒ have not been transmitted as

i. ☒ applicant chose not to make amendments under PCT Article 19.
Date of mailing of Search Report (from form PCT/ISA/210.): 06/08/1998

ii. ☐ the time limit for the submission of amendments has not yet expired. The amendments or a statement that amendments have not been made will be transmitted before the expiration of the time limit under PCT Rule 46.1.

6. ☐ A translation of the amendments to the claims under PCT Article 19 (38 U.S.C. 371(c)(3)):

a. ☐ is transmitted herewith.

b. ☐ is not required as the amendments were made in the English language.

c. ☐ has not been transmitted for reasons indicated at point 5(c) above.

7. ☒ A copy of the international examination report (PCT/IPEA/409)

☒ is transmitted herewith.

☐ is not required as the application was filed with the United States Receiving Office.

8. ☐ Annex(es) to the international preliminary examination report

a. ☐ is/are transmitted herewith.

b. ☐ is/are not required as the application was filed with the United States Receiving Office.

9. ☐ A translation of the annexes to the international preliminary examination report

a. ☐ is transmitted herewith.

b. ☐ is not required as the annexes are in the English language.

10. ☒ An oath or declaration of the inventor (35 U.S.C. 371(c)(4)) complying with 35 U.S.C. 115

a. ☐ was previously submitted by applicant on _____.
Date

b. ☐ is submitted herewith, and such oath or declaration

i. ☐ is attached to the application.

ii. ☐ identifies the application and any amendments under PCT Article 19 that were transmitted as stated in points 3(b) or 3(c) and 5(b); and states that they were reviewed by the inventor as required by 37 C.F.R. 1.70.

iii. ☒ will follow.

II. Other document(s) or information included:

11. ☒ An International Search Report (PCT/ISA/210) or Declaration under PCT Article 17(2)(a):

a. ☒ is transmitted herewith.

b. ☐ has been transmitted by the International Bureau.
Date of mailing (from form PCT/IB/308): _____.

c. ☐ is not required, as the application was searched by the United States International Searching Authority.

d. ☐ will be transmitted promptly upon request.

e. ☐ has been submitted by applicant on _____.
Date

12. ☐ An Information Disclosure Statement under 37 C.F.R. 1.97 and 1.98:

a. ☐ is transmitted herewith.

Also transmitted herewith is/are:

☐ Form PTO-1449 (PTO/SB/08A and 08B).

☐ Copies of citations listed.

b. ☐ will be transmitted within THREE MONTHS of the date of submission of requirements under 35 U.S.C. 371(c).

c. ☐ was previously submitted by applicant on _____.
Date

13. ☐ An assignment document is transmitted herewith for recording.

A separate ☐ "COVER SHEET FOR ASSIGNMENT (DOCUMENT) ACCOMPANYING NEW PATENT APPLICATION" or ☐ FORM PTO 1595 is also attached.

_____

_____

_____

14. ☒ Additional documents:

a. ☐ Copy of request (PCT/RO/101)

b. ☒ International Publication No. WO 98/32675

i. ☒ Specification, claims and drawing

ii. ☐ Front page only

c. ☒ Preliminary amendment (37 C.F.R. § 1.121)

d. ☐ Other

_____

_____

_____

15. ☒ The above checked items are being transmitted

a. ☒ before 30 months from any claimed priority date.

b. ☐ after 30 months.

16. ☐ Certain requirements under 35 U.S.C. 371 were previously submitted by the applicant on _____, namely:

_____

_____

_____

_____

_____

AUTHORIZATION TO CHARGE ADDITIONAL FEES

WARNING: *Accurately count claims, especially multiple dependant claims, to avoid unexpected high charges if extra claims are authorized.*

☒ The Commissioner is hereby authorized to charge the following additional fees that may be required by this paper and during the entire pendency of this application to Account No. 02-3869.

☒ 37 C.F.R. 1.492(a)(1), (2), (3), and (4) (filing fees)

WARNING: *Because failure to pay the national fee within 30 months without extension (37 CFR § 1.495(b)(2)) results in abandonment of the application, it would be best to always check the above box.*

☐ 37 C.F.R. 1.492(b), (c) and (d) (presentation of extra claims)

NOTE: Because additional fees for excess or multiple dependent claims not paid on filing or on later presentation must only be paid or these claims cancelled by amendment prior to the expiration of the time period set for response by the PTO in any notice of fee deficiency (37 CFR 1.492(d)), it might be best not to authorize the PTO to charge additional claim fees, except possible when dealing with amendments after final action.

☐ 37 C.F.R. 1.17 (application processing fees)

WARNING: *While 37 CFR 1 17(a), (b), (c) and (d) deal with extensions of time under § 1.136(a), this authorization should be made only with the knowledge that: "Submission of the appropriate extension fee under 37 CFR 1.136(a) is to no avail unless a request or petition for extension is filed." Notice of Nov. 5, 1985 (1060 O.G. 27).*

☐ 37 C.F.R. 1.18 (issue fee at or before mailing of Notice of Allowance, pursuant to 37 C.F.R. 1.311(b))

NOTE: *Where an authorization to charge the issue fee to a deposit account has been filed before the mailing of a Notice of Allowance, the issue fee will be automatically charged to the deposit account at the time of mailing the notice of allowance. 37 CFR 1.311(b).*

NOTE: *37 C.F.R. 1.28(b) requires "Notification of any change in loss of entitlement to small entity status must be filed in the application . . . prior to paying, or at the time of paying . . . issue fee." From the wording of 37 CFR 1.28(b): (a) notification of change of status must be made even if the fee is paid as "other than a small entity" and (b) no notification is required if the change is to another small entity.*

☐ 37 CFR 1.492(e) and (f) (surcharge fees for filing the declaration and/or filing an English translation of an International Application later than 30 months after the priority date).

John M. Kilcoyne

SIGNATURE OF ATTORNEY

Reg. No.: 33,100

John M. Kilcoyne

(type or print name of attorney)

Tel. No.: (908) 904-2431

Bristol-Myers Squibb Company
100 Headquarters Park Drive

P.O. Address

Skillman, New Jersey 08558

Docket No. CV0244

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re

Application of : Waring et al. Examiner :

Serial No.: Art Unit :

Filed : Herewith

For : Multi-Dose Wound Gel

Assistant Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

S I R:

Before examining this application, please amend it as follows:

In the Claims

Cancel claims 11 and 12.

Amend claims 3-9 as follows:

--3. (Amended) A vessel as claimed in claim 1 [or claim 2] wherein the gel comprises a natural gelling agent.

4. (Amended) A vessel as claimed in [any preceding] claim 1 wherein the gel comprises a glycol.

5. (Amended) A vessel as claimed in [any preceding] claim 1 wherein the gel comprises:

(a) from about 0.05% to 10% by weight of a natural gelling agent;

(b) from about 1.0% to 10% by weight of a hydrocolloid;

(c) from about 5.0% to 30.0% by weight of an alkylene glycol; and

(d) at least 50% by weight of water.

6. (Amended) A vessel as claimed in [any preceding] claim 1 wherein the gel is sterile.

7. (Amended) A vessel as claimed in [any preceding] claim 1 wherein the vessel contains multiple doses of wound gel.

8. (Amended) A method [Method] of making a barrier aerosol vessel comprising wound gel, the method comprising the steps of:

(i[I]) filling an inner container with gel, said inner container being contained within an outer casing container;

(ii) sealing the inner container with an opening valve; and

(iii) introducing a pressure medium between the inner container and the outer casing container.

9. (Amended) A method [Method] of making a barrier aerosol vessel comprising wound gel, the method comprising the steps of:

(i) filling an inner container with non-sterile gel, said inner container being contained within an outer casing container;

(ii) sealing the inner container with an opening valve;

(iii) sterilising the vessel and gel contained within it; and

(iv) introducing a pressure medium between the inner container and the outer casing container.--

Add New Claims

--13. A method for the treatment of wounds comprising discharging a wound gel from a barrier aerosol vessel containing the wound gel.

14. A method for the treatment of sinus wounds comprising discharging into a sinus cavity a wound gel from a barrier aerosol vessel containing the wound gel.--

Respectfully submitted,

John M. Kilcoyne

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908 904-2431

Express Mail mailing label number EM325661793US

Date of Deposit July 19, 1999

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231.

James Klein
(Typed or printed name of person mailing paper or fee)

(Signature of Person mailing paper or fee)

MULTI-DOSE WOUND GEL

This invention relates to a multi-dose wound gel. More particularly, this invention relates to a wound gel packaged in a multi-dose container, useful for treating wounds.

It is well known that the cleansing and debriding of wounds and the removal of wound exudate is important to the process of healing wounds. Commonly used wound dressings comprise gauze, foams, sponges, cotton wads or other fibrous materials. Gauze and other fibrous materials absorb fluids by capillary action with the disadvantage that when new tissue is formed as part of the healing process, it engulfs the fibres and is torn when the material is removed causing wound injury.

Various other materials have been used, such as gels hydrogels, granules and pastes to remove exudates from wounds. Certain wound gels are known to promote the healing of wounds. For instance they can keep the wound bed moist, cleanse the wound, debride necrotic matter by fluid donation and absorb exudate. Freshly generated tissue does not grow into the gel and thus injury on removal is avoided.

The gels are usually packaged in a tube and applied to the wound from the tube. The gels are usually in either a sterile or a preserved state. If packaged in a multi-dose tube there is a risk with some gels that once the tube is opened, bacteria will enter the tube and proliferate in the gel. For this reason some manufacturers include preservatives in the gel or package in single dose tubes. Some health care professionals are reluctant to introduce preservatives to a wound and so use single dose tubes containing sterile gel. This adds to the cost of the

product and results in wastage if the whole contents of the tube is not used. There is therefore a need for a multi-dose gel packaged in such a way that contamination is minimised once the packaging is opened.

We have now found that is possible to package a gel in multi-dose packaging which minimises contamination once opened. This is achieved by the use of a barrier aerosol.

Accordingly the invention provides a barrier aerosol vessel containing a wound gel for the treatment of wounds.

Aerosol barrier vessels are of the type where the product to be dispensed and the pressure generating media, ie the propellant, are maintained in isolation through separation on opposite sides of a barrier. This has many advantages in the context of wound gels. Firstly, because there is positive pressure in the container, the vessel can be made to be self-sealing. This aids maintenance of product sterility. Secondly, it is possible to use an aerosol using only one hand which makes application of the gel to the wound particularly easy. In the case of sinus wounds, where there is undermining of the tissue beneath the wound site and beyond its surface periphery, it is possible to insert the nozzle through the sinus to fill the cavity with gel. Thirdly, since the propellent is not mixed with the gel, the physical and chemical properties of the gel are not affected by being dispensed in this manner. It is therefore possible to use known gels which have a long clinical history with the advantages of being dispensed under pressure as described above.

Three main variants of barrier vessel exist. In a piston-type barrier vessel the barrier is a piston-like component that is mounted in the container in sliding relation to the inside surface of the container. The product to be dispensed is disposed on the valved side of the piston and

the propellant, which generates pressure within the container, is on the opposite side of the piston. Examples of piston-type barrier packs are described in US 3,033,923, 3,756,476 and 3,929,132.

In a second variant of an aerosol barrier vessel, a flexible collapsible inner container is affixed within an outer container opening either to the aerosol discharge valve or to the bead of the container opening. Patents which illustrate a barrier vessel of this variant are described in US 3,788,521, 3,896,970 and 4,067,499.

In a third variant the barrier vessel is an unfolding cup-shaped barrier wherein the barrier has an outer wall terminating in a sealing flange, said outer wall being disposed contiguous to the inner wall of the container. The inner wall of the barrier is initially folded within the outer wall, the inner wall terminating in an end closing portion. The barrier is contained in a valved aerosol container and sealed at the joint formed between the sidewall and the bottom end closure of the container. Product is admitted through the valved opening of the container and propellant through a port in the bottom end closure of the container. Actuation of the valve reduces the pressure in the product compartment and results in the inner wall of the barrier unfolding from within the outer wall of the barrier and causing the end-closing portion of the inner wall of the barrier to advance and thereby urge the product toward the discharge port. This type of barrier vessel is illustrated in US 3,109,463 and WO 96/02439.

The barrier aerosol vessel preferably used in the present invention is of the second or third type and comprises an inner container which contains the gel sealed by an opening valve with a discharge port for discharging the gel, an outer casing container covering the inner container and a

pressure medium interposed between the inner container and the outer casing container. The use of this type of container enables the inner container to be filled with non-sterile gel while assembled in the outer casing container, sealed by the valve and then sterilised by steam sterilisation. The pressure medium can then be introduced without compromising the sterility of the product. If a non-barrier type of aerosol were used then sterilisation would not be possible due to the presence of propellant in the wound gel.

Preferably the inner container is made of a thin flexible material such as plastic or metal foil, although metal foil is especially preferred to maintain sterility if a sterile gel is used. The outer casing container is also preferably metal such as aluminium which is pressure resistant. The outer container is preferably formed by compression moulding, thermoforming or the like, the inside provided with an inner protective coating and primed and the base provided with a valve to enable the container to be pressurised once the inner container has been filled and sealed. The inner container is preferably sealed by a valve which comprises a cup and a discharge port and closes off the outer container.

A barrier vessel suitable for use in the present invention is illustrated in the following figures:

Figure 1 is an elevation in section of one embodiment of the invention.

Figure 2 is a perspective view of the vessel of the invention in use.

An example of a barrier aerosol vessel (2) suitable for use in the present invention is shown in Figure 1 and comprises an inner container (4) which contains a gel (6) sealed by

an opening valve (8) for discharging the gel (6), an outer casing container (10) covering the inner container (4) and a pressure medium (12) interposed between the inner container (4) and the outer casing container (10). The outer casing container is provided with a sealable port (14) to enable the pressure medium (12) to be introduced. The opening valve (8) comprises a cup (16) and discharge port (18). The whole of the opening valve (8), including cup (16) and port (18) will conventionally be covered with an applicator (not shown). Depression of which by the user causes the gel to exit the port (18) into a conventional nozzle or an extension nozzle depending on the use. Such nozzles can be separately packaged for single use.

Figure 2 shows the aerosol vessel of the invention in use. In this view an applicator has been placed on the opening valve to aid application of the gel to a wound.

When the gel is to be dispensed the valve (8) is actuated, the pressure medium acts to collapse the inner container (4) and gel (6) flows from the discharge port (18) of valve (8).

The gel for use in the present invention is preferably a hydrocolloid gel and comprises a cellulose derivative, water and a polyol component. Such gels are described in EP-A-576523. More preferred is a gel comprising:

(a) optionally from about 0.05% to 10% by weight of a natural gelling agent;
(b) from about 1.0% to 10% by weight of a hydrocolloid;
(c) from about 5.0% to 30.0% by weight of a glycol and
(d) at least 50% by weight of water.

The most preferred composition contains 0.1% pectin, 3.4% sodium carboxymethyl cellulose, 15% propylene glycol and 81.5% water. Such gels are described in EP-A-567311 and EP-A-666081.

The natural gelling agent is preferably selected from pectin, alginic acid and salts thereof, carageenan, tragacanth, acacia, locust bean gum, guar gum, starch, agar and gelatin. More preferably the pectin is pectin with a high ester content derived from citrus peel consisting chiefly of the partial methyl esters of polygalachronic acid (approximately 65% of the carboxyl groups are esterified). Representatives of the pectin useful in the gel composition is that marketed under the name GENU pectin type VIS-L by Copenhagen Pectin. The natural gelling agent is preferably present in an amount from 0.05% to 1.0% by weight.

The hydrocolloid is preferably selected from sodium carboxymethyl cellulose, methyl cellulose, hydroxypropylmethyl cellulose, hydroxyethyl cellulose, hydroxymethylcellulose, hydroxypropyl cellulose, carboxyvinyl polymer and salts thereof, poloxamer for example Pluronic F127, xanthan gum, povidone, modified starches, and guar derivatives. The carboxymethyl cellulose is preferably sodium carboxymethyl cellulose present in an amount from about 2.0% to 4.5% by weight. The preferred sodium carboxymethyl cellulose is a high viscosity sodium carboxymethyl cellulose (typically in the range 2000 - 4500 cps as measured by Brookfield LV Viscometry of a 1% solution, oven dry basis, 25°C and spindle 4/30 rpm.

The glycol can be an aryl or alkylene glycol, preferably selected form the group of glycerol, polyethylene glycol, panthanol, and sorbitol. If the glycol is an alkylene glycol it is preferably propylene glycol present at from about 10.0% to 20.0% by weight.

The water used in the gel is preferably purified and pyrogen free water and is present in an amount sufficient to bring the total composition up to 100% by weight.

Various optional ingredients can also be included in the gel composition such as preservatives eg, methylhydroxybenzoate and propylhydroxybenzoate. In addition, the wound gel composition can, if desired, contain small amounts (effective amounts) i.e. less than 5%, of pharmacologically active ingredients. For example, an antibiotic or antimicrobial agent such as metronidazole, silver sulphadiazine, neomycin or penicillin, and antiseptic agent such as povidone iodine, and anti-inflammatory agent such as hydrocortisone or triamcinolone acetonide, or a skin protective agent such a zinc oxide can be included.

We have found that the invention performs particularly well if the gel has a viscosity of from 150 to 800 Pas as determined by Viscolog model MRV8 viscometer and a helical drive unit and PD spindle rotating at 2.5 rpm. Gels packaged in this way have been found to have particularly homogeneous viscosity due to the uniformity of the package compared to that found in tubes or other less symmetrical dispensing devices.

The barrier vessel containing a wound gel of the invention may be made by the method described in EP 0418724 or EP 0017147 to Lechner GmbH. The vessel may be sealed by a valve having a cup and discharge port, particularly of the type CA38F/39F ex Rexam Dispenser, Portsmouth UK, although valves having a gasket able to withstand steam sterilisation would be suitable for producing a sterile product.

We have also found that the rate at which gel is dispensed may be altered by altering the applicator nozzle size. Thus it is possible to change the applicator in order to get fast release or slow release of the gel which may be important for some wounds.

The invention is illustrated by the following non-limiting examples.

Example 1

Gel composition	% by weight
Pectin	0.1%
Sodium carboxymethyl cellulose	3.4%
Propylene glycol	15.0%
Purified water	81.5%

Pectin (0.2g) was added to purified water (163.0g) in a beaker and heated to 50 - 60°C with constant stirring until the pectin dissolved. Propylene glycol (30.0g) was added and sodium carboxymethyl cellulose (6.8g) was gradually added with constant mixing. A hydrocolloid gel (200g) was produced.

Example 2

The gel from example 1 was used to fill the inner container of a barrier aerosol vessel and a valve having a cup and discharge port applied to seal the vessel. The filled container was terminally steam sterilised for 30 minutes at 121C. The vessel was then removed to a clean room and an applicator fitted to the valve and the outer container gassed to pressurise the gel.

Example 3

The barrier aerosol vessel containing gel prepared as in Example 2 was subjected to a microbial challenge. A mixed microbial suspension (S.aureus, E.coli and C. albicans - all typical wound bacteria) was prepared at a concentration of 1x105/ml and inoculated into the first 2cms of gel contained in the nozzle of the vessel. The inoculated canned gel was then left to stand at room temperature for

a period of 7 days and then sampled. This mimics clinical use. After sampling the gel was re-inoculated with the microbial suspension and sampled after a further 7 days. Sampling was achieved by 10 fold dilution plating out appropriate dilutions onto pre-dried TSA plates. The plates were incubated at 35C for 24/48 hours prior to counting.

The results of the assay demonstrated a 5 log reduction in each of the three challenge organisms over days 0-7 and 7-14. These results show that micro-organisms do not proliferate in the gel contained in the barrier vessel. This makes the combination of gel and barrier vessel suitable for a multi-dose sterile product.

CLAIMS

1. A barrier aerosol vessel containing a wound gel for the treatment of wounds.

2. A vessel as claimed in claim 1 wherein the gel comprises a hydrocolloid.

3. A vessel as claimed in claim 1 or claim 2 wherein the gel comprises a natural gelling agent.

4. A vessel as claimed in any preceding claim wherein the gel comprises a glycol.

5. A vessel as claimed in any preceding claim wherein the gel comprises:
(a) from about 0.05% to 10% by weight of a natural gelling agent;
(b) from about 1.0% to 10% by weight of a hydrocolloid;
(c) from about 5.0% to 30.0% by weight of an alkylene glycol and
(d) at least 50% by weight of water.

6. A vessel as claimed in any preceding claim wherein the gel is sterile.

7. A vessel as claimed in any preceding claim wherein the vessel contains multiple doses of wound gel.

8. Method of making a barrier aerosol vessel comprising wound gel the method comprising the steps of:
(I) filling an inner container with gel, said inner container being contained within an outer casing container;
(ii) sealing the inner container with an opening valve; and

(iii) introducing a pressure medium between the inner container and the outer casing container.

9. Method of making a barrier aerosol vessel comprising wound gel the method comprising the steps of:

(i) filling an inner container with non-sterile gel, said inner container being contained within an outer casing container;

(ii) sealing the inner container with an opening valve;

(iii) sterilising the vessel and gel contained within it; and

(iv) introducing a pressure medium between the inner container and the outer casing container.

10. A multiple dose, sterile wound gel contained within an aerosol vessel.

11. Use of a barrier aerosol vessel containing a wound gel for the preparation of a wound care product for use in the treatment of wounds.

12. Use of a barrier aerosol vessel containing a wound gel for the preparation of a wound care product for use in the treatment of sinus wounds.

FIG. 1

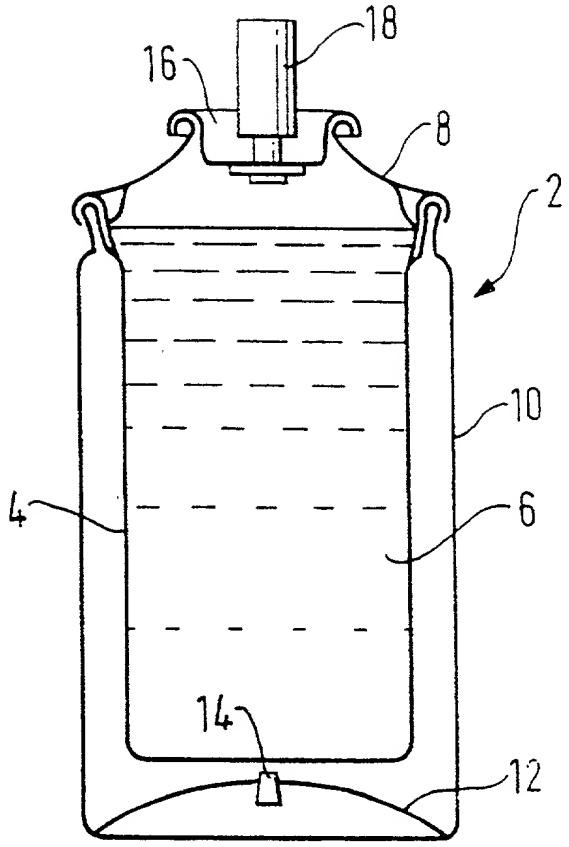
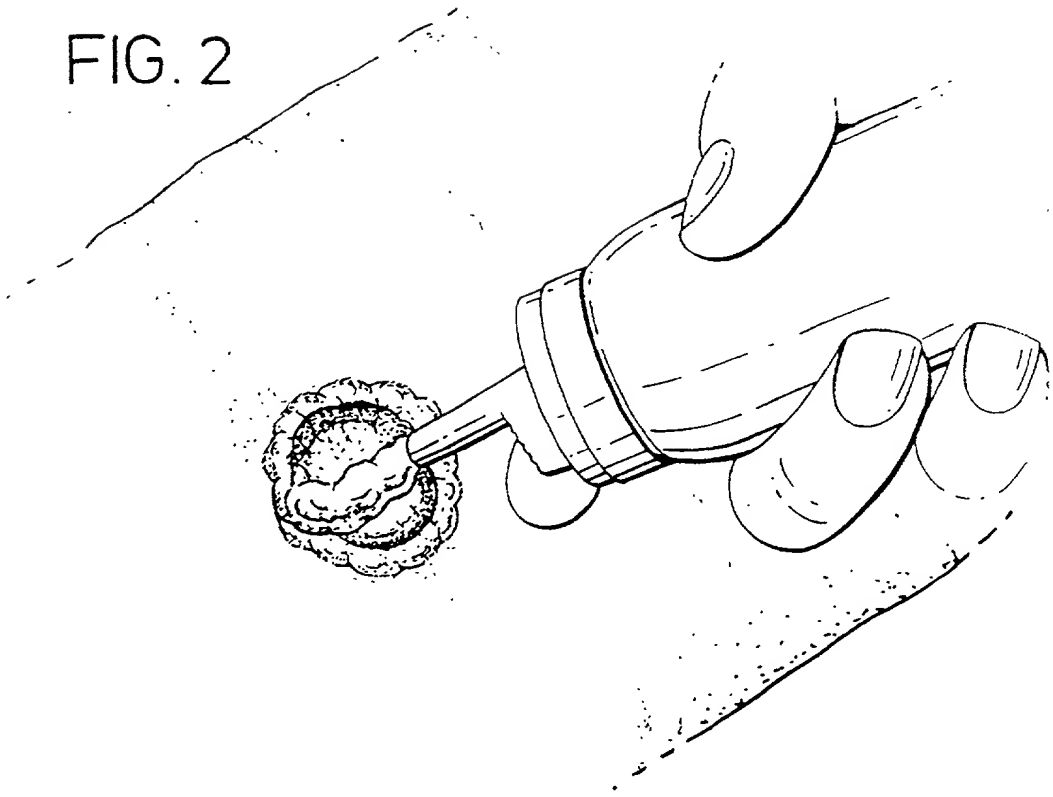


FIG. 2



Attorney Docket No. CV0244

COMBINED DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that: My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed for which a patent is sought on the invention Multi-Dose Wound Gel the specification of which

[ ] is attached hereto
[X] was filed on July 19, 1999 as
Application Serial No. 09/341,821

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56(a).

I hereby appoint the following attorneys and/or agents to prosecute this application and to transact all business to the Patent and Trademark Office connected therewith: Theodore R. Furman, Jr., Reg. No. 30,942; John M. Kilcoyne, Reg. No. 33,100; Stuart E. Krieger, Reg. No. 28,731. Address all correspondence to ~~T.R. Furman~~, c/o Bristol-Myers Squibb Company, 100 Headquarters Park Drive, Skillman, New Jersey 08558. Telephone (908) 904-2372.

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

PRIORITY FOREIGN APPLICATION(S)

Number	Country	Filed (day/month/year)	Priority Claimed (Yes or No)
PCT/EP98/00526	GB	22.01.1998	Yes
9701552.3	GB	25.01.1997	Yes

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

(Application S.N.)	(Filing Date)	(Status) (patented, pending, abandoned)

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

1 - 0

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